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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/746,361	11/08/96	ANDERSON	D 012712-256

EXAMINER

HM12/0116

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ART UNIT	PAPER NUMBER
1644	31

DATE MAILED: 01/16/01

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 11/2/00

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 29-37 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 29-37 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. Applicant's amendment, filed 11/2/00 (Paper No. 30), is acknowledged.

Claims 29-37 are pending and being acted upon presently
Claims 1-28 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 11/2/00 (Paper No. 30).
The rejections of record can be found in the previous Office Action (Paper No. 27).

3. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 previously sent in Paper No. 7.
Formal figures will be submitted upon indication that this application is allowable.

4. Claims 29-37 stand rejected over by de Boer et al. (U.S. Patent No. 5,747,034) and Linsley et al. (U.S. Patent No. 5,770,197) in view of art-known procedures and motivation to generate recombinant antibodies (e.g. humanized, chimeric or primatized) for diagnostic and therapeutic regimens as acknowledged on pages 15-20 and 24-27 of the specification (e.g. Newman et al. Biotechnology, 1992).

Applicant's arguments in conjunction with Ex parte Kranz, filed 11/2/00 (Paper No. 30), have been fully considered but are not found convincing as they apply to rejection under obviousness for B7-1-specific antibodies which inhibit binding for CD28 but not CTLA-4.

Applicant's arguments and the examiner's rebuttal are essentially the same as of record.

Applicant argues that the claims are drawn to a novel and non-obvious antibody that specifically binds to B7.1 (CD80) and which inhibits the binding of B7.1 antigen to CD28, but which antibody does not inhibit the binding of B7.1 to CTLA-4.

Applicant submits that this specificity is distinguished from the prior art anti-B7.1 antibodies which inhibited bot the B7.1:CD28 and B7.1:CTLA-4 interactions.

Applicant asserts that neither prior art reference even remotely infers the existence of any antibodies possessing the novel and non-obvious binding properties of the subject invention.

Applicant argues that the prior art does not provide sufficient motivation and expectation of success in achieving the claimed specificity.

Applicant argues that Linsley is limited to its teachings to the BB-1 antibody which is specific to B7.1 and inhibits the interaction of B7.1 to CTLA-4 and CD28.

In contrast to applicant's assertions'; Linsley et al. ('197) teach the role of the B7 molecules as well as CTLA-4 and CD28 in cell signaling and various molecules including antibodies to block their functions (see entire document).

Also, Linsley et al. teach anti-B7 antibodies may be used to bind to B7 to inhibit interactions of CD28-positive "or" CTLA-positive T cells with B7 positive cells (see column 15, paragraph 7).

By teaching the inhibition of CD28 or CTLA interactions in the alternative; one of ordinary skill in the art at the time the invention was made would have had an expectation of success in generating B7.1-specific antibodies that could block B7:CD28 interactions OR B7:CTLA-4 interactions.

Again; it is noted that de Boer et al. indicate that while the B7 molecules as well as CTLA-4 and CD28 are involved in cell interactions and signaling; there are distinct differences in their properties as well as the binding and inhibitory properties of various molecules. See Detailed Description of the Invention, including columns 5-6. Therefore, de Boer clearly recognizes differences between CD28 and CTLA-4 as they apply to their interaction with B7 at the time the invention was made.

As acknowledged previously; applicant's arguments in conjunction with the signed Anderson declaration under 37 C.F.R. § 1.132, filed 1/18/00, distinguish the binding specificity of the de Boer and Linsley et al. antibodies of the prior art

Again, applicant has argued that B7 binds both CTLA-4/CD28, which have a high degree of homology; therefore antibodies that bind B7 and inhibit its interaction with CD28 would also be expected to inhibit interaction with CTLA-4.

However, given the known exquisite specificity of antibodies and that CTLA-4/CD28 are distinct molecules albeit homologous; one of ordinary skill in the art at the time the invention was made would have been motivated to select recombinant B7.1-specific antibodies as diagnostic and therapeutic agents in treating human immunoregulatory disorders.

Applicant assert that the claimed antibodies should have the unexpected nature of being more efficient in inhibiting immune responses since the natural regulatory interaction of CTLA-B7 will not be disturbed.

However, applicant has not provide objective evidence to support this more efficient immunoregulatory role.

In contrast to applicant's assertion of being more efficient; it is noted that there is a complexity to inhibiting the CD28:B7 costimulatory pathway with blocking agents. See Daikh et al. J. Leukoc. Biol. 62: 156-162, 1997 for a review. For example, CTLA-4Ig which binds both B7.1 and B7.1 is generally more efficient as an immunoregulatory molecule than antibodies that inhibit B7.1 or B7.1 in the alternative. Also, targeting B7.1 or B7.2 specifically can lead to different effects in different systems, that is, each specificity can block, exacerbate or have not effect on immunosuppressing the immune reactions depending on the model investigated (see pages 159-160; Effects of Selective Blockade of B7-1 or B7-2 on Autoimmunity). Therefore, it is not readily apparent that blocking B7.1:CD28 interactions and not B7.1:CTLA-4 interactions would be more efficient immunoregulatory pathway.

One of ordinary skill in the art at the time the invention was made would have been motivated to select anti-B7 antibodies with differential properties of blocking binding to CD28 and CTLA-4 for various detection, diagnostic and therapeutic uses. Given that CD28/CTLA-4 were known to structurally and functionally distinct; the ordinary artisan would have had an expectation of success in generating antibodies which inhibit B7-CD28 binding and not B7-CTLA-4 binding at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

5. Claims 29-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,113,898. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are species/subgeneric of the instant claimed antibodies/composition and that the patented antibodies are the exemplified antibodies of the instantly claimed antibodies.

Claims 29-37 are directed to an invention not patentably distinct from claims 1-11 of commonly assigned U.S. Patent 6,113,898 for the reasons above.

Commonly assigned U.S. Patent No. 6,113,898, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78© to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

Applicant's amendment, filed 11/2/00 (Paper No. 30), indicates that a Terminal Disclaimer will be submitted when there is an indication of allowability.

6. Claims 29-37 are provisionally rejected 35 U.S.C. § 102(e) as anticipated by or 35 U.S.C. § 103 as being obvious over Anderson et al. (U.S. Patent No. 6,113,898).

Copending application Serial No. 08/487,550 has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. § 102(e) if patented. This provisional rejection under 35 U.S.C. § 103 is based upon a presumption of future patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 C.F.R. § 1.132 that any unclaimed invention disclosed in the copending application was derived from the inventor of this application and is thus not the invention "by another", or by a showing of a date of invention prior to the effective U.S. filing date of the copending application under 37 C.F.R. § 1.131.

This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Anderson et al. teach B7-1-specific antibodies which appear to have the same or nearly the same properties encompassed by the instant claims. The burden is on the applicant to establish a patentable distinction between the claimed and referenced antibodies.

Applicant's arguments, filed 11/2/00 (Paper No. 30), have been fully considered but are not found convincing.

Applicant argues that this rejection does not qualify as prior art under 102(e) because the claimed subject matter finds implicit suport in the earlier application, which is relied upon for priority herein.

However, the filing date of the instant claims is deemed to be the filing date of the instant application, i.e. 11/8/96, as the parent application does not provide written support for the instant claims.

Also, it is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Applicant is invited to provide objective evidence that the U.S. Patent No. 6,113,898, filed as USSN 08/487,550, provide written description for the instant claims.

U.S. Patent No. 6,113,898 is by another. See MPEP 2136.04.

Applicant's arguments are not found persuasive.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

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